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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/894,356	08/18/97	ASHIKARI T	001560-308

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EXAMINER	
ZAGHMOUT, O	
ART UNIT	**PAPER NUMBER**
1638	26

DATE MAILED: 10/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/894,356	Ashikari et al
Examiner	**Group Art Unit**
Ousama Zaghmout	1638

☒ Responsive to communication(s) filed on *Aug 10, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-3, 5-12, 20, and 22-52* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3, 5-12, 20, and 22-52* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ See attachment #1.

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Detailed Office Action

I. The request filed on 08/10/2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/894,356 is acceptable and a CPA has been established. An action on the CPA follows.

II. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

III. The amendment filed 08/10/2000 have been received and entered [Paper No. 24].

IV. The submitted sequence listing has been received and entered the databases at the PTO.

V. Status of the claims:

Claims 4, 13-19 and 21 have been canceled (Paper No. 24).

Claims 1, 5-8, 20, 22-24, 27, 28, 33-34 and 42-45 have been amended (Paper No. 24).

Claims 46-52 have been newly added.

Claims 1-3, 5-12, 20, 22-52 are pending.

Claim Rejections-35 U.S.C. 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-3, 5-12, 25-32, 36-38, 42-52 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The gene, as claimed, has the same characteristics and utility as those found naturally in the genome or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. V. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 91980).

Amendment of claims 1 and 28 by inserting --An isolated— prior to the word "gene" would obviate the rejection.

Claim Rejections - 35 U.S.C. § 112

Ist Paragraph

I. WRITTEN DESCRIPTION:

1. Claims 1-3, 9-12, 20, 22, 23-27, 46-47 are rejected under 35 U.S.C. 112, first paragraph because specification does not contain a written description of the claimed

invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed for the reasons of record stated in the previous Office Action mailed 2-12-1999 and 02/10/2000.

Applicants state that the scope of the claims invention has been amended to recite that the gene as claimed encodes a protein which transfers an aromatic acyl group to flavonoid (paragraph 4, page 7 of the REMARKS). Applicants further cite in Tables A and B (page 8 of the REMARKS) the relationship between clones obtained from various origins and the substrate specificity of enzymes expressed from these clones. Applicants state that the cloned genes encode enzymes which are structurally different, but have a common activity and that the amino acid sequence homology between the proteins encoded by the genes cloned in the present invention is low despite the fact that these proteins have a common activity. Applicants argue that the specification does provide guidance as how one of skill in the art would isolate genes which encode enzymes which have the same activity as the enzymes encoded by the nucleotide sequences set forth in SEQ ID NOS: 1-6 and that the molecular techniques have been described in the specification as in page 5 or Example 3 (second paragraph, page 9 of the REMARKS).

These arguments have been carefully considered, but not found persuasive for a number of reasons.

First: The specification of the instant invention can only be used by those skilled in the art to isolate nucleotide sequences which encode one single enzyme from a number of plant species, namely anthocyanin acyltransferase from the anthocyanin pigment. However, the pigment anthocyanin has more than one acyltransferase enzyme, depends on the chemical structure of the enzyme (e.g., anthocyanin 5-aromatic acyltransferase). The question is whether nucleotide sequences of other acyltransferases are the same or similar to those exemplified in the specification. Neither the specification nor the prior art provides any teaching regarding the other nucleotide sequences. Moreover, the specification does not teach if the nucleotide sequences which encode the aromatic acyl group transfer activity are conserved among all proteins which exhibit said activity. The specification does not teach that any gene as claimed has a conserved sequence or consensus sequence is in fact unique to a gene which encodes a protein which transfers an aromatic acyl group to flavonoid.

The teaching disclosed in the Examples cited above can be used to isolate nucleotide sequences which encode one protein from a number of plant species. Since not all proteins which exhibit acyltransferases activity are identical, the nucleic acid sequence and amino acid sequence are not expected to be identical either. In order to be able to claim the genus, Applicants are required to isolate nucleotide sequences of different proteins which exhibit acyltransferases activity, not of the same protein, from a number of plant species. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual

cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that a patent specification contain a written description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art to make and use" the invention.

Second. Applicants disclose in Example 11 of the specification an in Table A and B in the REMARKS that sequences of the amino acid sequences are highly conserved between these proteins which transfer an aromatic acyl group to flavonoid. The Office response is that all of these sequences relate to a single protein as described above namely anthocyanin acyltransferase. These amino acid sequences are highly conserved for the same protein isolated from a number of plant species. However, the claimed subject matter encompasses more than one single protein with acyltransferase activity of the anthocyanin pigment. Those of skill in the art can use primers form SEQ ID: 1-6 to isolate only additional sequence that are very similar to sequences of SEQ ID: 1-6, not of different sequences. Applicants have not shown that this is not the case in the instant application. Subsequently, the specification of the instant application satisfies only the written description for one gene which encodes a specific acyltransferase of the anthocyanin pigment.

Third: Claiming the subject matter "gene" by function does not adequately satisfy the written description requirement. Such function does not distinguish the claimed gene from others, except by function, and a definition by function does not suffice to define the gene because it is only an indication of what the gene does, rather than what it is. To satisfy the

written description for a genus, the Applicants must supply more than the mere function of the gene or the protein in which the nucleotide sequence encodes. Third. The function " transfers an aromatic acyl group to flavonoid" appearing in the specification does not satisfy the written description requirement, and that the specification does not provide any information regarding the relevant structure or physical characteristics of the nucleotide sequence encoding any gene which transfers an aromatic acyl group to flavonoid or the actual nucleotide. In addition, Applicants have disclosed only the nucleotide sequence of the coding region of the anthocyanin acyltransferase gene. Applicants have not disclosed the full length of the promoter or any other regulatory elements such as introns, enhancers, activators of the gene. Fourth: Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling. The separateness of the two requirements has been emphasized in the biotechnology area by two cases. Both cases involved interference's in which the count in question related to a strand of DNA. In one case Fiers v. Sugamo[25 USPQ2d 1601 (Fed. Cir. 1993], :"An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself."

Based on the above mentioned arguments above and in the previous office action, the rejection of these claims for not satisfying the written description is maintained.

II. SCOPE OF ENABLEMENT:

1. Claims 1-3, 5-12, 20, 22-52 are rejected under 35 U.S.C. 112, first paragraph for the reasons of record detailed in the previous Office actions for because the specification is enabled only for isolation of the nucleotide sequence identified in SEQ ID NOs: 1-6 which encode a protein having aromatic acyl group transfer activity, for the construction and introduction of the acyltransferase gene into petunia.

Applicants argue that the specification describes how one of skill in the art could obtain nucleotide sequences from a variety of plant species, wherein said nucleotide sequences encode a protein which transfers an aromatic acyl group to flavonoid. In that respect, Applicants state that the specification is enabled for the isolation of a number of nucleotide sequences as set forth in SEQ ID NO:1-6. However, this was not persuasive to overcome the rejection for a number of reasons:

First: The Examiner pointed out in the previous Office actions that the specification does disclose only the isolation of the nucleotide sequences identified in SEQ ID NOs: 1-6 which contain nucleotide sequences that encode a protein having aromatic acyl group transfer activity, and for the construction and introduction of the acyltransferase gene into petunia. The specification describes various homologous sequences to the nucleotide sequence which encodes anthocyanin acyltransferase, not any acyltransferase which transfers the acyl group to

any flavonoid. Applicants have neither not shown if these genes are the same for all acyltransferases of the anthocyanin pigment. None of these genes were expressed at the plant level. The specification clearly states in lines 31-32, page 39 that " the result indicates that the gene of acyltransferase of gentians could be introduced into the rose". The specification does not teach if acyltransferases gene expressed at the plant level to a level whereby the desired phenotype was obtained. As explained in the previous Office action, that integration of a gene does not mean that an expression of a phenotype from said gene will be obtained.

B. To further show that invention as claimed is not enabled by the specification, The Examiner have disclosed a number of nucleotide sequences which they are very similar to the nucleotide sequence set forth in SEQ ID NO: 22. As shown in the disclosed attachment, none of these sequences can be used as a primer to enable the the isolation of any protein that mediate the transfer of any acyl group to the flavonoid since none of these sequences fall into that category (Please see attachment No. 1). One wishing to practice the invention is left to proceed through trial-and-error to see what will work and what will not.

C. To further show that invention as claimed is not enabled by the specification, the specification does not teach if a method for stabilizing a pigment will be produced in a transgenic plant that express any of the claimed genes. Those skilled in the art recognize that stability of the pigment is controlled by a number of factors other than the expression of a gene, such as light, heat, pH, hydrogen peroxide and enzymes such as peroxidase. For example, López-Serrano et al teach that stability of pigment is affected by the level of

hydrogen peroxide and peroxidase (see at least Abstract, J Agric Food Chem 1999 Mar 47:3 824-827), factors which are not even remotely related to a protein which mediates the transfer of acyltransferase to flavonoid. As such, it is unpredictable if the invention as claimed would be enabled by the disclosed specification.

Based on the forgoing, these claims are rejected because the specification fails to describe how to make and use the invention as claimed.

2nd Paragraph

I. The rejection of claim 6 under 112 second paragraph for the recitation of " with part " which has been withdrawn in view of the amendment of the claim.

Applicants the art.

II. The rejection of claims 22 and 33 under 35 USC 112 second paragraph as being redundant. Has been withdrawn in view of the Applicants' argument.

III. Claim 25 remains rejected under 35 USC 112 2nd as being vague for the recitation of " which has its colored controlled". Furthermore, Applicants are requested to clarify the language in lines 1-2 of the claim. The claim reads now that the color has been controlled by "its progeny".

Applicants argue that the claimed subject matter is clear. Applicants have recited these statements from the claim. However, Examiner maintains that the claimed subject matter is not written in a clear and concise manner. Therefore, a clarification is requested.

IV. Claims 5-6, 42-45 are rejected under 112 second paragraph as being vague and indefinite for the recitation of the term "consensus sequence" as it is not clear from the specification if the nucleotide sequence encompassed by the claims are those present in SEQ ID NOS: 1-6, 21 22, or any nucleotide sequence that is present in these sequences. As such, the metes and the bounds of the claimed subject matter are not fully and completely defined in a clear and concise manner.

Furthermore, Applicants have used the terms "conserved" and "consensus" sequence interchangeably (See fourth paragraph in page 12 of the REMARKS). Those skilled in the art would recognize that those terms do not mean the same meanings. Consensus Sequence describes the nucleotide sequence (within a DNA molecule) which gives the most common nucleotide at each position (along that sequence of that DNA molecule), for those instances (in certain organisms) where a (usually small) number of variations in nucleotide sequences can occur (e.g., for a given nucleotide sequence such as a promoter sequence). In contrast, conserved sequence is a term used to describe a domain (region or a sequence) of a molecule that remains the same in all, or most, variations of an organism.

Conclusion

NO claims are allowed.

Future Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell Ph.D., can be reached on (703) 308-4310. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

PAULA HUTZELL
SUPERVISORY PATENT EXAMINER
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Ousama M-Faiz Zaghmout Ph.D.

October 18, 2000